

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Paragraph at page 5, lines 5-12:

~~Figure 1 depicts~~ Figure 1A, 1B, 1C and 1D depict the amino acid sequence alignment between the cellulose synthases encoded by the following: (a) nucleotide sequence derived from garden balsam clone ids.pk0029.h10 (SEQ ID NO:26), (b) nucleotide sequence derived from wheat clone wlmk4.pk0015.a11 (SEQ ID NO:30), and (c) nucleotide sequence from *Arabidopsis thaliana* (NCBI GenBank Identifier (GI) No. 2827143; SEQ ID NO:33). Amino acids which are conserved among all and at least two sequences with an amino acid at that position are indicated with an asterisk (*). Dashes are used by the program to maximize alignment of the sequences.

Paragraph at page 16, lines 25-29:

~~Figure 1 presents~~ Figure 1A, 1B, 1C and 1D present an alignment of the amino acid sequences set forth in SEQ ID NOs:26 and 30 and the *Arabidopsis thaliana* sequence (NCBI GI No. 2827143; SEQ ID NO:33). The data in Table 6 represents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:26 and 30 and the *Arabidopsis thaliana* sequence (NCBI GI No. 2827143; SEQ ID NO:33).

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 23-35 are now pending, with Claim 23 being the sole independent claim.

Applicants have attached hereto replacement drawings to amend the view numbers to refer to Figures 1A, 1B, 1C and 1D. The corrections to the view numbers necessitate amending the Brief Description of Drawings and Examples in the specification to refer to these new view numbers.

Turning now to the Office Action mailed April 23, 2003:

Regarding the question about the Sequence Listing and the region of SEQ ID NO:29 that encodes SEQ ID NO:30, the total length of the isolated cDNA consists of 3626 bp (SEQ ID NO:29) and is believed to contain a single open reading frame of 3243 bp (from 60-3302) encoding a functionally complete protein of 1080 amino acids (SEQ ID NO:30). Applicants note that there is an ATG codon at position 60-62 (not at position 59-61 as indicated in the Office Action) and the termination codon is at position 3300-3302 (TAG).

Regarding the Section 112, 1st paragraph written description rejection. Applicants respectfully traverse.

Under the PTO Written Description Guidelines, the written description requirement is met with disclosure of "functional characteristics when coupled with a known or disclosed correlation between function and structure." Guidelines, 66 Fed. Reg. at 1106.

Applicants submit that there is a well-known correlation between the cellulose synthase activity disclosed and claimed in the instant specification and cellulose synthase protein (and corresponding nucleic acid) structure.

Applicants believe the following references to be representative of the knowledge of one of ordinary skill in the art:

Delmer (*Ann. Rev. Plant Physiol. Plant Mol. Biol.* 50:245-276 (1999)) ("Delmer")
Holland et al. (*Plant Physiol.* 123:1313-1323 (2000)) ("Holland")
Richmond et al. (*Plant Physiol.* 124:495-498 (2000)) ("Richmond et al.")
Richmond (*Genome Biology* 1(4):reviews3001.1-3001.6 (2000)) ("Richmond")

Each of these references, except Holland which was cited in the originally-filed IDS, are cited in a Supplemental IDS filed simultaneously herewith.

Cellulose synthases described to date have a number conserved structural features:

1. At the amino terminus of the protein is an amino acid domain that bears some resemblance to a zinc finger or LIM transcription factor. See, e.g., Richmond et al., page 496, column 1.
2. Within this zinc finger domain is a strictly conserved sequence motif, known as the 'CXXC' motif. This motif has the following single-letter amino-acid code, where X is any amino acid:

CX₂CX₁₂FXACX₂CX₂PXCX₂CXX₅GX₃CX₂C

See, e.g., Richmond, page 2, column 1.

3. There are three conserved aspartic acid (D) residues that are widely spaced (a single D, followed by a DXD, and then a third D). See, e.g., Delmer, page 258, Figure 2; and Richmond, page 2, column 2]
4. Following the third aspartic acid is another conserved motif (QXXRW) that is thought to form the active site together with the three aspartic acid residues. See, e.g., Delmer, page 258, Figure 2; and Richmond et al., page 496, column 2.
5. There are eight putative transmembrane helices – two in the amino terminus and six in the carboxy terminus. See, e.g., Delmer, page 266, Figure 3; and Holland, page 1313, column 2.

Appendix A, attached hereto, is a Clustal V alignment of SEQ ID NO:30 of the instant claims and *Arabidopsis thaliana* cellulose synthase (GI 2827143).

The above 1-4 conserved structural features for these two sequences are identified in Appendix A by boxes and labels.

Furthermore, PSORT (www.psort.nibb.ac.jp; PSORT program was coded by: Kenta Nakai, Ph.D., Human Genome Center, Institute for Medical Science, University of Tokyo, Japan (knakai@ims.u-tokyo.ac.jp)) was used with the instant SEQ ID NO:30 to assign the putative transmembrane domains.¹ The following output

¹ PSORT employs Klein et al. method ("ALOM", also called as KKD) to detect potential transmembrane segments (P. Klein, M. Kanehisa, and C. DeLisi, *Biochim. Biophys. Acta*, 815:468 (1985)). It attempts to identify the most probable transmembrane segment from the average hydrophobicity value of 17-residue segments, if any. It predicts whether the segment is a transmembrane segment (INTEGRAL) or not (PERIPHERAL) comparing the discriminant score (reported as 'value') with a threshold parameter pre- defined to 0.0 for bacteria ('threshold'). For an integral membrane protein, position(s) of transmembrane segment(s) are also reported. Their length

illustrates eight putative transmembrane helices – two in the amino terminus and six in the carboxy terminus:

| ALOM program | count:8 | value:-9.34 | threshold:0.5 |
|-----------------------|---------|--------------------------|---------------|
| INTEGRAL Likelihood = | -9.34 | Transmembrane 1054 -1070 | (1050 -1075) |
| INTEGRAL Likelihood = | -5.79 | Transmembrane 903 - 919 | (897 - 922) |
| INTEGRAL Likelihood = | -5.47 | Transmembrane 874 - 890 | (868 - 896) |
| INTEGRAL Likelihood = | -4.51 | Transmembrane 990 -1006 | (989 -1008) |
| INTEGRAL Likelihood = | -4.25 | Transmembrane 309 - 325 | (307 - 326) |
| INTEGRAL Likelihood = | -3.40 | Transmembrane 281 - 297 | (277 - 298) |
| INTEGRAL Likelihood = | -1.28 | Transmembrane 939 - 955 | (939 - 955) |
| INTEGRAL Likelihood = | -0.00 | Transmembrane 1021 -1037 | (1021 -1037) |

Given this known correlation between cellulose synthase activity and protein structure, Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence having 80% sequence identity to SEQ ID NO:30 while still retaining cellulose synthase activity.

Thus, the combination of the Applicants' disclosure and the known correlation of function and amino acid sequence structure renders the claims in compliance with the written description requirement.

Withdrawal of the Section 112, 1st paragraph written description rejection is respectfully requested.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

is fixed to 17 but their extension, i.e., the maximal range that satisfies the discriminant criterion, is also given in parentheses. The discrimination step mentioned above is continued after leaving out the segment till there remains no predicted transmembrane segment. The item 'count' is the number of predicted transmembrane segments.

The Commissioner is authorized to charge Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company) for any requisite fees due or to credit any overpayment.

Applicants' undersigned may be reached at the below-listed numbers.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'J. Kenneth JounG', with a stylized flourish at the end.

J. KENNETH JOUNG
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REGISTRATION NO. 41,881
TELEPHONE: 302-992-4929
FACSIMILE: 302-892-1026

Dated: 23 October 2003

Attachments: Appendix A
Replacement Drawings (4 sheets)

Appendix A

#1 and #2 - zinc finger resembling LIM and 'CXXC' motif

| | | | |
|-----|--|---|----------------------|
| 1 | M.....K..... | CQIC.D..G.T.DGD.F.ACD.C.FPVCRPCYE.ERK.G.Q | Consensus #1 |
| 1 | MDGADAI-KSGRHGAGDV | CGICADGLGTTLDGDFITACDVCFPVCRCPCYEHERKEGTQ | BB1170USCIPSeqIdNo30 |
| 1 | MESEGETAGKPMKNIVPQT | CGICSPNVGKTVPGDRFVACDICSFPVCRPCYEYERKDSNQ | GI 2827143 |
| 60 | ..C.QCKT.YKR..GSPAIG...D..AD.G..FNYP.....QK.KI..RM..W.... | | Consensus #1 |
| 61 | ACLOCKTKYKRHRGSPAIRGSEFGDDDDADDGS-DFNYPASGTEDOKOKIADRMRSWRMNT | | BB1170USCIPSeqIdNo30 |
| 60 | SCPOCKTRKRLKGSIPAIPGDKDEDEGLADEGTVEFNYP-----QKEKSERMLGWHLTR | | GI 2827143 |
| 119 | G.....G.P.YD.....E.....P..T..Q..SGE...ASP.....S.T... | | Consensus #1 |
| 119 | GSSGNVGHPRKVDSGELIGLSKYDSGEIIRGVPSVTNSQ-MSGELIPGASPDHHMSPPTGNI | | BB1170USCIPSeqIdNo30 |
| 115 | GKGEEMGEPOYDK-----FVSHNHLPRLTSRQDTSGEFSAASPERLSVSSITAG | | GI 2827143 |
| 178 | ..R.P.....VN.SPN.....GNVAMKERVDGWMKQ.K..P.....S.....R. | | Consensus #1 |
| 164 | SRRAPEPY-MNHSPNPSSRETSSTGNVAMKERVDGWMKQDKGAIPTMTNGTSLAPSEGRA | | BB1170USCIPSeqIdNo30 |
| 237 | GKRLPYSSDVNQSPNRRIVDPVGLGNVAMKERVDGWMKQEKNTGPV---STQAASERG | | GI 2827143 |
| 237 | ..DIDAST.....ALNDE.RQPLSRKV.I.SS.INPYRMVI.LRLV.L..FLHYR.TN | | Consensus #1 |
| 237 | AIDIDASTEYNMEDALINDETROBLSRKVPFASSKINPYRMVIVLRIVLVLSIFLHYRLTN | | BB1170USCIPSeqIdNo30 |
| 237 | GVDIDASTDILADEALINDEARCPLSRKVSLPSSRINPYRMVIMRLVILCLFLHYRITN | | GI 2827143 |



Appendix A

| | | |
|-----|--|----------------------|
| 297 | PV.NA..LWL.SVICEIWFALSWILDQFPKWEP.NRETYLDRALRYDREGESPQLAAVD | Consensus #1 |
| 280 | 310 320 330 340 350 360 | |
| 297 | PVRNATPLWLLSVICETWFAALSWITBQTPKWFPIINRETYLDRALRYDREGESPQLAAVD | BB1170USCIPseqIdNo30 |
| 280 | PVPNAFALWLVSVICEIWFALSWILDQFPKWEPVIRETYLDRALRYDREGESPQLAAVD | GI 2827143 |
| 357 | IFVSTVDPLKEPP.VTANTVLSILAVDYPVDKVSQYV.D | Consensus #1 |
| 340 | 370 380 390 400 410 420 | |
| 357 | IFVSTVDPLKEPPITVANTVLSILAVDYPVDKVSQYVSDGASMTTFOALAESEFARKW | BB1170USCIPseqIdNo30 |
| 340 | IFVSTVDPLKEPPLVITANTVLSILAVDYPVDKVSQYVFDGASMTTSESLAESEFARKW | GI 2827143 |
| 417 | VPEF.KKY.IEPPAPE.YF.KIDYLKDKVQ.SFVKDRRAAMKREYEEFKIRINALVSKALK | Consensus #1 |
| 400 | 430 440 450 460 470 480 | |
| 417 | VPEVKKKYDTEPPRAPEEYVFCQKIDYLKDKVQPSFVKDRRAAMKREYEEFKIRINALVSKALK | BB1170USCIPseqIdNo30 |
| 400 | VPECKKYSTEPPRAPEWYFAAKIDYLKDKVQTSFVKDRRAAMKREYEEFKIRINALVSKALK | GI 2827143 |
| 477 | .PEEGW.MQDGTWPNGNNT.DHPGMIQVFLG.GGLD.EGNELPRLVVSREKRPGFQHH | Consensus #1 |
| 460 | 490 500 510 520 530 540 | |
| 477 | VPEEGWIMQDGTWPNGNNTDRHPGMIQVFLGSHSGGLDTEGNEELPRLVVSREKRPGFQHH | BB1170USCIPseqIdNo30 |
| 460 | CPEEGWVMQDGTWPNGNNTGDRHPGMIQVFLGQNGGLDAEGNEELPRLVVSREKRPGFQHH | GI 2827143 |
| 537 | KKAGAMNALVRVSAVLTING...LN | Consensus #1 |
| 520 | 550 560 570 580 590 600 | |
| 537 | KKAGAMNALVRVSAVLTINGQYMINLDGDHYIINNSKAVREANCFILMDPNLGPQVCYVQEPQ | BB1170USCIPseqIdNo30 |
| 520 | KKAGAMNALVRVSAVLTINGPFIINLDGDHYIINNSKALREANCFILMDPNLGPQVCYVQEPQ | GI 2827143 |

#3 - conserved D

#3 - conserved D



Appendix A

597 RFDGID.NDRYANRNTVFEDINLRGLDGIQGPVYVGTGCVFNRTA.YGYEPPIK.K..KP Consensus #1
 580 610 620 630 640 650 660
 RFDGIDRNDRYANRNTVFFDINLRGLDGIQGPVYVGTGCVFNRTAIYGYEPPIKAK--KE
 RFDGIDKNDRYANRNTVFFDINLRGLDGIQGPVYVGTGCVFNRTALYGYEPPIKVKKHKE
 BB1170USCIPSeqIdNo30
 GI 2827143

655 ..L..LCGG..K.....K..SDKKKS..H.DS.VPVFN.LDIEEGVEGAGFDDEK..LMS Consensus #1
 640 670 680 690 700 710 720
 GFLASLGGGKKKASKSKSKRRSSDKKSNKHVDSSVPVFNLEDEEGVEGAGFDDEKSVLMS
 SLSSKLCGGSRKKNSKAKKESDKKSGRHTDSTVPVFNLDIEEGVEGAGFDDEKALLMS
 BB1170USCIPSeqIdNo30
 GI 2827143

715 QMSLEKRFQSA.FVASTIME.GGVP.S.TPE.LLKEAIVHISCGYEDKS.WG.EIGWIY Consensus #1
 700 730 740 750 760 770 780
 QMSLEKRFQSA.FVASTIME.GGVP.QSSTPESLLKEAIVHISCGYEDKSEWGTIIGWIY
 QMSLEKRFQSA.FVASTIME.GGVP.PSAPPENLLKEAIVHISCGYEDKSDMGWPIGWIIY
 BB1170USCIPSeqIdNo30
 GI 2827143

775 #3 - conserved D #4 - conserved QXXRW
 760 GSVTEIDILTGFKMHARGWRS.YCMPK.PAFKGSAPINLSDRLNQVLRWALGSVEILFSRH Consensus #1
 790 800 810 820 830 840
 GSVTEIDILTGFKMHARGWRS.YCMPK.PAFKGSAPINLSDRINQVLRWALGSVEILFSRH
 GSVTEIDILTGFKMHARGWRS.YCMPK.PAFKGSAPINLSDRINQVLRWALGSVEILFSRH
 BB1170USCIPSeqIdNo30
 GI 2827143

835 CP.WYGY.GRLKFLERFAY.NTTIYP.TS.PLL.YC.L.A.CL.T..FI.P.ISN.ASIW Consensus #1
 820 850 860 870 880 890 900
 CPELWYGYGGRLKFLERFAY.NTTIYP.TS.PLLVYCI.LPAICLLTGKFIIMEEISNLSASIW
 CPIWYGYNGRLKFLERFAY.NTTIYP.TS.PLLMYCTLLAVCLFTNQFIIPEQISNIASIW
 BB1170USCIPSeqIdNo30
 GI 2827143



Appendix A

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| 895 | F. | L | F | L | S | I | F | A | T | G | I | L | E | M | R | S | G | V | G | I | D | E | W | R | N | E | Q | F | W | V | I | G | . | S | A | H | L | F | A | V | F | Q | G | . | L | K | V | L | A | G | I | D | T | N | F | | |
| 880 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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| 955 | T | V | T | S | K | A | . | D | E | . | G | D | F | A | E | L | Y | . | F | K | W | T | L | L | I | P | P | T | . | L | I | . | N | . | V | G | V | V | A | G | . | S | Y | A | I | N | S | G | Y | Q | S | W | G | P | L | F | G | K |
| 940 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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| 1015 | L | F | F | A | F | W | I | V | H | L | P | F | L | K | G | L | M | G | R | Q | N | R | T | P | T | I | V | . | V | W | . | V | L | L | A | S | I | F | S | L | L | W | V | R | . | D | P | F | T | . | R | . | G | P | . | I | . |
| 1000 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| | | | | | | |
|------|---|---|---|---|---|---|
| 1075 | T | G | G | I | N | C |
| 1060 | E | C | G | I | N | C |

Consensus #1: When all match the residue of BB1170USCIPSeqIdNo30 show the residue of BB1170USCIPSeqIdNo30, otherwise show ''

Shade (with black at 40% fill) residues that match BB1170USCIPSeqIdNo30 exactly.

